REMARKS

Amendments

Claims 17-19 and 24 have been amended. Claims 20-23 and 25 have been canceled. The amendments to the claims do not constitute new matter and are completely supported throughout the specification and originally filed claims. More particularly, support for the amendments can be found, for example, at page 51, lines 1-8, of the specification and in Figures 4-5.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 17-19 and 24 are pending in the instant application.

Rejections

Rejection under 35 U.S.C. § 101

The Examiner has rejected claims 17-25 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility. Applicant respectfully traverses the rejection. However, Applicant believes the rejection has been overcome in light of the claim amendments and arguments below.

Claims 17-25 are directed toward a transgenic mouse having a disruption in a low density lipoprotein-related protein 5 gene, wherein the mouse exhibits retinal degeneration, increased anxiety or hypoactivity, to a method of producing the transgenic mouse, and to a cell or tissue obtained from the transgenic mouse.

The Examiner has alleged that Applicant has not provided a specific or substantial use for the transgenic mouse exhibiting the claimed phenotypes, and that there does not exist in the art such a use. The Examiner has based his conclusions on an alleged lack of a link between the phenotypes exhibited by the claimed mouse and any specific disease or to a disease caused by a disruption in humans. Applicant asserts that such a link does exist, and is generally accepted within the art of transgenic and knockout mice. More particularly, Applicant believes that a link does exist between a phenotype of decreased time in the central region of an open field and

anxiety, between decreased total distance traveled and hypoactivity, and between retinal degeneration in a mouse and human. Applicant believes that a link would be recognized by the skilled artisan in light of the homology between the mouse and human genomes, and the general acceptance that gene function in the mouse is related to and representative of that of human. It is generally viewed in the art that when genes are knocked out or disrupted in mice, as in the present invention, the resulting phenotype reveals or is representative of the function of that gene. In the present case, the phenotype of the transgenic mice comprising disrupted LRP5 genes, specifically increased anxiety, hypoactivity or retinal degeneration, indicates a role for LRP5 in these conditions, and establishes the utility of the mice as models for such conditions or disorders, and for discovering treatments for such conditions or disorders.

Despite Applicant's belief that such a link is well-established in the art, Applicant is not aware of any requirement for expressly stating that a link exists in order to satisfy the utility requirements set forth in 35 U.S.C. § 101, nor is it believed that the establishment of such a link is required for patentability of the transgenic mouse as claimed. Applicant submits that in order to satisfy these requirements, the specification must assert a specific and substantial utility that is credible to a skilled artisan, or the utility of the claimed invention must be apparent to the skilled artisan. See MPEP § 2107.

Applicant believes that he has asserted several uses for the transgenic mice claimed. These include but are not limited to use as models for disease (*e.g.* a model of retinal degeneration, anxiety or hypoactivity), for identifying agents that ameliorate disease symptoms, for identifying agents that affect or modulate a phenotype caused by the gene disruption, or for determining the specificity of an agent targeting the LRP5 gene (see, for example, page 17, lines 23-24, page 18, lines 8-19 and lines 24-28, and page 19, lines 7-11, of the specification). Further, Applicant submits that these utilities of the claimed mouse would be immediately apparent to the skilled artisan, even absent Applicant's disclosure. However, even in the absence of a link between the phenotype(s) of the claimed mouse and disruption of LRP5 in humans, as discussed above, a link between LRP5 disruption and the claimed phenotypes in the mouse is clearly established. The skilled artisan would see the utility or value of the transgenic mouse for studying or investigating conditions related to LRP5, in this case anxiety, hypoactivity and eye disorders such as retinal degeneration in the mouse, for discovering or developing treatments for

these conditions in mice or related mammals, or for studying the role of LRP5 in such conditions. Each of these are clearly "real world" uses for the claimed transgenic mice.

In view of the amendments to the claims and arguments set forth above, Applicant has overcome the rejection of the claims under 35 U.S.C. § 101, and respectfully requests withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph

Enablement: The Examiner has rejected claims 17-25 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the transgenic mice having retinal degeneration, increased anxiety or hypoactivity as a result of the alleged lack of either a specific or substantial asserted utility or a well-established utility set forth in the above utility rejection. Applicants respectfully traverse the rejection. However, in view of the amendments to the claims and arguments in response to the utility rejection set forth above, Applicants submit that the rejection under 35 U.S.C. § 112, first paragraph, has been overcome.

In addition, the Examiner has asserted that the claims to not provide a nexus between the disruption in the LRP5 gene and the lack or production of LRP5 or the phenotypes of retinal degeneration, increased anxiety, or hypoactivity. The Examiner further asserts that the phenotypes of increased anxiety and hypoactivity are relative and that the claims must recite to what they are compared. Applicant traverses this aspect of the rejection. However, Applicant submits that this aspect of the rejection is overcome in light of the amendments to the claims.

Written Description: The Examiner has also rejected claims 17-25 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant traverses the rejection.

Specifically, the Examiner states that the specification does not support the amendments made to the claims in the previous response. More particularly, the Examiner asserts that the specification only teaches a mouse having retinal degeneration as a result of a disruption in LRP5, not a mouse having a disruption in LRP5 **and** retinal degeneration as broadly claimed. Applicants disagree that the claimed mouse is not supported by the specification. However, the amendments made to the claims overcome this aspect of the rejection in that the claims now recite that the retinal degeneration is a result of the disruption in LRP5.

The Examiner also asserts that support cannot be found for the limitation of "increased anxiety", the specific phenotypes in claims 18, 19, 22 and 23, for obtaining tissue or for heterozygous disruptions. Applicant submits that support for these claims can be found throughout the specification and originally filed claims. More specifically, support for the transgenic mouse exhibiting increased anxiety, and more particularly decreased time in central region of an open field as in claims 18 and 22, can be found at page 51, lines 3-5, page 24, lines 11-15 of the specification, and in Figure 4. Support for the phenotype recited in claim 19 can be found at page 51, lines 6-8 of the specification and Figure 5. Claims 20-23 have been canceled. Therefore, Applicant believes that the written description rejection has been overcome.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 17-25 were rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses the rejection. Claims 20-23 have been canceled.

Regarding claims 17 and 24, the Examiner states that the claims are indefinite because they do not clearly set forth that the disruption of LRP5 causes the lack of production of LRP5 or the retinal degeneration, increased anxiety or hypoactivity. Applicant's amendments of claims 17 and 24 overcome this aspect of the rejection.

In addition, claims 17 and 24 are asserted to be indefinite because they allegedly do not set forth to what the mice are being compared with regard to increased anxiety and hypoactivity phenotypes. As amended, claims 17 and 24 recite to what the parameters of increased anxiety and hypoactivity are compared.

With regard to claims 18 and 19, the Examiner asserts that it is unclear whether the field test is related to the increased anxiety or hypoactivity in claim 17 or is in addition. Applicants have amended claims 18 and 19 to make it clear that the open field test is related to the increased anxiety or hypoactivity phenotypes recited in claim 17.

Further, regarding use of the term "characterized" in claims 18 and 19, the Examiner asserts that it cannot be determined if the claim is limited to the phenotype recited or if the claim encompasses mice having a phenotype related to the phenotype recited. As claims 18 and 19 no longer recite the term "characterized", this aspect of the rejection no longer applies.

Claim 21 has been asserted as indefinite because it cannot be determined if the mice have a homozygous or heterozygous disruption. Applicants have overcome this issue by cancellation of claim 21.

The Examiner's rejection of claims 22 and 23 as lacking antecedent basis for the terms "increased anxiety" and "hypoactivity" is no longer relevant as a result of the cancellation of these claims.

In light of the amendments to the claims, each of the Examiner's rejections under 35 U.S.C. § 112, second paragraph, have been overcome. Applicant respectfully requests withdrawal of the rejection.

Rejection under 35 U.S.C. § 102

Claim 20 was rejected under 35 U.S.C. § 102(b) as being anticipated by Weaver (1997, *J Biol Chem,* Vol 272, pg 14372-14379). The Applicant respectfully traverses the rejection. However, in light of the cancellation of claim 20, the rejection under 35 U.S.C. § 102 is no longer relevant. Applicant submits that pending claims 17-19 and 24 are not anticipated by the teachings of Weaver.

Double Patenting

The Examiner has objected to claim 25 under 37 C.F.R. § 1.75 as allegedly being a substantial duplicate of claim 17. Although Applicant disagrees with the Examiner's conclusion, claim 25 has been canceled. Applicant requests the objection be withdrawn.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-193.

Respectfully submitted,

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